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Racial Differences in Quantitative Measures of Area and Volumetric Breast Density

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Abstract

Background: Increased breast density is a strong risk factor for breast cancer and also decreases the sensitivity of mammographic screening. The purpose of our study was to compare breast density for black and white women using quantitative measures.
Methods: Breast density was assessed among 5282 black and 4216 white women screened using digital mammography. Breast Imaging-Reporting and Data System (BI-RADS) density was obtained from radiologists' reports. Quantitative measures for dense area, area percent density (PD), dense volume, and volume percent density were estimated using validated, automated software. Breast density was categorized as dense or nondense based on BI-RADS categories or based on values above and below the median for quantitative measures. Logistic regression was used to estimate the odds of having dense breasts by race, adjusted for age, body mass index (BMI), age at menarche, menopause status, family history of breast or ovarian cancer, parity and age at first birth, and current hormone replacement therapy (HRT) use. All statistical tests were two-sided.
Results: There was a statistically significant interaction of race and BMI on breast density. After accounting for age, BMI, and breast cancer risk factors, black women had statistically significantly greater odds of high breast density across all quantitative measures (eg, PD nonobese odds ratio [OR] = 1.18, 95% confidence interval [CI] = 1.02 to 1.37, $P = .03$, PD obese OR = 1.26, 95% CI = 1.04 to 1.53, $P = .02$). There was no statistically significant difference in BI-RADS density by race.
Conclusions: After accounting for age, BMI, and other risk factors, black women had higher breast density than white women across all quantitative measures previously associated with breast cancer risk. These results may have implications for risk assessment and screening.

Breast density is a strong risk factor for breast cancer; women with high breast density have four to six times increased risk of breast cancer compared with women with low density (1–12). This higher risk is partly explained by the fact that dense tissue can mask tumors, making mammography less sensitive among women with dense breasts (13) while tumor size at diagnosis also increases and prognosis worsens with increasing breast density (14). In addition, hormonal risk factors and genetics may contribute to breast density (15–19). How these and other factors influence breast density and form the pathways by which density increases breast cancer risk are areas of active research.

Breast density has taken on added importance recently. As of March 2016, 25 states have passed legislation mandating notification of breast density in order to identify women that may benefit from supplemental screening, encompassing

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nearly two-thirds of screening-eligible US women. It is unclear what effect such policy will have on breast cancer disparities. Racial differences in breast density would have implications for breast cancer risk assessment and could lead to different screening practices for women in many states.

Compared with white women, black women have higher breast cancer mortality, are diagnosed with later stage disease, and have higher incidence of poor prognosis and triple-negative breast cancers (20,21). Studies investigating racial differences in breast density have had mixed results (22–31). Comparisons of breast density by race may be confounded by factors such as age (32), body mass index (BMI) (33), use of hormone replacement therapy (HRT) (34), and reproductive factors (32,35), all of which are known to impact breast density and to differ substantially by race, particularly BMI (36). Not all studies have fully controlled for these factors, making it difficult to identify whether there are racial differences in breast density at the population level and whether these are fully accounted for by BMI or other hormonal factors.

An additional complication is that there are several ways to measure breast density. Breast density is typically estimated clinically by radiologists' qualitative visual assessment using the American College of Radiology Breast Imaging-Reporting and Data System (BI-RADS) categories (37), but this measure has limited reproducibility (38–42). Quantitative breast density measures, such as percent density, can be measured using semi-automated software such as Cumulus (43,44), which provides a continuous score and has been used in many studies. Fully automated quantitative tools have also been developed to improve reproducibility of density measurement (45,46). These various methods quantify the amount of dense breast tissue in different ways. The two-dimensional (2D) assessments of breast density from a conventional mammogram can provide an estimate of the dense tissue (dense area) or the percent of breast tissue that is dense (area percent density). However, while these 2D area measures may capture measures of density that are predictive of cancer risk and the "masking effect" because of increased breast density, such measures may not fully capture the actual volume of dense tissue in the breast. Toward this end, three-dimensional (volumetric) estimations of both dense area and percent density have also been developed to more accurately quantify fibroglandular tissue (8,47). All of these measures have been associated with breast cancer risk, though the magnitude of the associations differs across measures and studies (46). Lastly, most prior studies have used film rather than digital mammograms, which are now the standard of care (48).

The purpose of our study was to investigate the association of race with breast density by comparing novel quantitative breast density measures for black and white women while also taking into account differences in age, BMI, hormone use, and reproductive factors.

ARTICLE

Methods

Study Population

From September 1, 2012, through August 31, 2013, a total of 11 141 women underwent routine screening mammography at the Hospital of the University of Pennsylvania, of whom 11 117 had raw digital mammogram images available for analysis. We selected 10 216 women identified in electronic medical records as white or black/African American. We excluded women with a prior history of breast cancer (n = 96, 0.9%), women missing weight or height (n = 485, 4.8%), women with breast implants (n = 109, 1.1%), women missing a BI-RADS breast density category in their screening reports (n = 17, 0.2%), and those for whom quantitative density measurements could not be obtained (n = 10, 0.1%). This resulted in a final study population of 9498 individual women. Self-report of demographic and reproductive breast cancer risk factors including age, menopause status, prior biopsy, atypical hyperplasia, age at first birth, age at menarche, family history of breast or ovarian cancer, and use of hormone replacement therapy (HRT) were available from a mammography screening questionnaire administered as part of routine practice. Weight and height were extracted from electronic medical records recorded on the screening date if available and if not from within one year prior to screening date. The study was HIPAA-compliant and approved by the Institutional Review Board of the University of Pennsylvania, and a waiver of informed consent was granted for this review of existing clinical data.

Breast Density Measurements

Visual BI-RADS breast density estimates given by the interpreting radiologist were obtained from mammography screening reports. The estimates were based on the ACR BI-RADS Atlas 4th Edition (37) definitions and given as an overall assessment of a woman's breast density corresponding to standard categories of 1) fatty, 2) scattered densities, 3) heterogeneously dense, and 4) extremely dense.

For each woman, raw (ie, "For Processing") bilateral, two-view screening digital mammograms were retrospectively analyzed. From these images, two types of quantitative mammographic density measures were obtained: area-based and volume-based measures.

Dense area was measured on a per-image basis using fully automated, publicly available software (Laboratory for Individualized Breast Radiodensity Assessment [LIBRA], v.1.1.0) (Figure 1) (49), which has been previously validated against Cumulus (45) as well as breast cancer (50). The details of the LIBRA algorithm have been previously described (45). Briefly, LIBRA first identifies the air-breast boundary and the edge of the pectoral muscle (when present). Within the breast region, the algorithm identifies the dense areas of the mammogram using fuzzy c-means clustering and support vector machine classification. Finally, absolute breast area (cm^2) and absolute dense area (cm^2) are derived, and area percent density (%) is obtained from the ratio of absolute dense area to the total breast area. A per-woman score of each measure was generated by averaging estimates from each image.

Mammographic dense volume was obtained using a commercially available software package (Quantra, v.2.0). Based on an adaptation of the validated Highnam and Brady method (51,52) for digital mammography, the software estimates the fraction of each pixel that contains fibroglandular tissue using known tissue x-ray attenuation properties (ie, adipose vs fibroglandular). An estimate of the absolute dense volume is then obtained by summing the fibroglandular tissue thickness of all pixels within the breast, and an estimate of breast volume is obtained by summing the overall thickness of each pixel within the breast, accounting for the breast edge. An estimate of volume percent density is derived from the ratio of these two measures. Finally, as with area density above, a per-woman composite score of each volume density measure was generated by averaging the density estimates from each image. A description of the breast density measures used in our study is provided in Table 1.

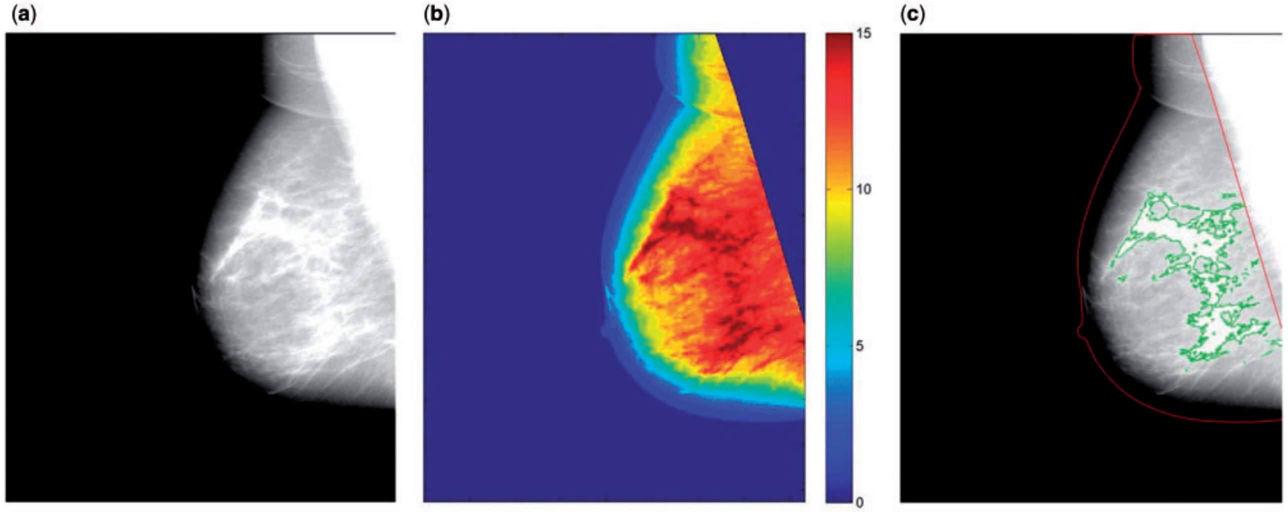

Figure 1. A representative example of the Laboratory for Individualized Breast Radiodensity Assessment breast density estimation algorithm applied on a digital mediolateral-oblique view mammogram from a black woman age 50 years with American College of Radiology Breast Imaging Reporting and Data System density category 2 breasts (ie, scattered densities). **A)** Original digital mammogram. **B)** Cluster-based identification or regions of similar density. **C)** Final dense tissue segmentation, corresponding to a dense area of 26.6 cm^2 and an area percent density of 13.0%.

Table 1. Breast density measures evaluated in the study

Breast density measure	Type of measurement	Source of measurement
BI-RADS density	Subjective	Radiologist interpretation on mammogram report
Dense area, cm^2	Quantitative, area based	LIBRA software*
Area percent density, %	Quantitative, area based	LIBRA software*
Dense volume, cm^3	Quantitative, volume based	Quantra software†
Volume percent density, %	Quantitative, volume based	Quantra software†

*University of Pennsylvania Center for Biomedical Image Computing and Analytics, https://www.cbica.upenn.edu/sbia/software/LIBRA/index.html. BI-RADS = American College of Radiology Breast Imaging Reporting and Data System; LIBRA = Laboratory for Individualized Breast Radiodensity Assessment.
†Quantra breast density assessment software, Hologic, Inc.

ARTICLE

Statistical Analysis

BMI was calculated from weight and height (53). Women missing menopause status (n = 790, 7%) were assumed to be premenopausal if younger than age 50 years and postmenopausal if age 50 years or older. Parity and age at first birth were categorized as nulliparous, older than 20, 20 to 24, 25 to 29, and 30 years or older. BI-RADS breast density was categorized as dense (heterogeneously dense or extremely dense) or nondense (almost entirely fatty or scattered fibroglandular densities). Characteristics of the study sample were compared by race using the t test and Chi-square tests, and density measures were compared by race using the Wilcoxon rank-sum test. Scatter plots of log-transformed BMI and log-transformed quantitative breast density measures were compared by race. Linear regression lines were fit, and the interaction of race and BMI on density was tested using linear regression with the inclusion of cross-product terms for the race-BMI interaction. For multivariable analysis, quantitative breast density measures above the median were categorized as dense and below the median as nondense based on the median value of each measure in the full sample. Logistic regression was performed separately for each density measure to estimate the odds of having dense breasts by race, adjusted for the following factors: age, BMI (continuous), age at menarche, menopause status, family history (first-degree relative with breast or ovarian cancer), parity and age at first birth, and current HRT use. The interaction of race and BMI on the density measures was also tested in the logistic regression models by including cross-product terms and analyses stratified by BMI of less than 30 kg/m^2 (nonobese) and BMI of 30 kg/m^2 or greater (obese) were performed. All statistical tests were two-sided, with statistical significance level of an α value of .05. Analyses were performed using STATA 12 (StataCorp LP, College Station, TX).

Results

The study sample included 55.6% black (n = 5282) and 44.4% white (n = 4216) women (Table 2). The mean age was 57 years for both groups (white = 57.3 years, SD = 10.9; black = 57.0 years, SD = 11.0, P = .20). Black women had higher mean BMIs than whites (32.4 kg/m^2, SD = 7.6 vs 26.4 kg/m^2, SD = 7.6, P < .001). Women excluded because of missing BMI were similar to women with complete BMI data in terms of their age, race, BI-RADS breast density, and quantitative breast density measures. With the exception of menopause status, the distribution of breast cancer risk factors differed statistically significantly for black and white women.

Table 2. Descriptive characteristics of the study population (n = 9498)

Characteristic	White (n = 4216)	Black (n = 5282)	P*
Age, mean ± SD, y	57.3 ± 10.9	57.0 ± 11.0	.20
Age categories, No. (%)			
<40 y	130 (3.1)	89 (1.7)	<.001
40–49 y	1034 (24.5)	1517 (28.7)	
50–59 y	1351 (32.0)	1683 (31.9)	
60–69 y	1147 (27.2)	1258 (23.8)	
≥70 y	554 (13.1)	735 (13.9)	
BMI, mean ± SD	26.4 ± 6.0	32.4 ± 7.6	<.001
BMI categories, No. (%)			
<18.5 kg/m^2	96 (2.3)	37 (0.7)	<.001
18.5–24.9 kg/m^2	1975 (46.9)	728 (13.8)	
25.0–29.9 kg/m^2	1206 (28.6)	1425 (27.0)	
≥30 kg/m^2	939 (22.3)	3092 (58.5)	
Menopause status, No. (%)			
Premenopause	1374 (32.6)	1662 (31.5)	.24
Postmenopause	2842 (67.4)	3620 (68.5)	
Prior biopsy, No. (%)	1282 (33.4)	1133 (23.5)	<.001
Atypical hyperplasia, No. (%)	57 (1.4)	11 (0.2)	<.001
Age at first birth, No. (%)			
Nulliparous	1206 (28.6)	821 (15.5)	<.001
<20 y	172 (4.1)	1616 (30.6)	
20-24 y	573 (13.6)	1215 (23.0)	
25-29 y	815 (19.3)	543 (10.3)	
≥30 y	1091 (25.9)	403 (7.6)	
Missing/unknown	359 (8.5)	684 (13.0)	
Age at menarche, No. (%)			
7–11 y	576 (13.7)	927 (17.6)	<.001
12–13 y	1957 (46.4)	1969 (37.3)	
≥14 y	825 (19.6)	993 (18.8)	
Missing/unknown	858 (20.4)	1393 (26.4)	
Family history†, No. (%)	1046 (24.8)	952 (18.0)	<.001
Ever used HRT, No. (%)	1108 (26.3)	577 (10.9)	<.001
Current HRT use, No. (%)	263 (6.2)	76 (1.4)	<.001

*P values from two-sided *t* tests for continuous variables and Chi square test for categorical variables. BMI = body mass index; HRT = hormone replacement therapy.
†First-degree relative(s) diagnosed with breast or ovarian cancer.

When examining the unadjusted distributions of the different breast density measures for black and white women, differences were observed across most measures (Tables 3 and 4). Based on BI-RADS density, 22.0% of black women had density in the highest two categories (21.0% heterogeneously dense, 1.0% extremely dense) compared with 40.9% of white women (37.8% heterogeneously dense, 3.1% extremely dense, $P < .001$). When comparing quantitative measures, black and white women had similar levels of dense area (22.2 cm^2 vs 22.3 cm^2, $P = .24$), but black women had lower area percent density than white women (12.3% vs 17.1%, $P < .001$). Black women, however, had a greater volume of dense tissue (266.9 cm^3 vs 196.1 cm^3, $P < .001$) but lower volume percent density compared with white women (9.8% vs 11.6%, $P < .001$).

When scatter plots of quantitative density measures and BMI were examined (Supplementary Figure 1, available online), we observed differences in the association of BMI with quantitative density measures for white and black women, and the interaction of race and BMI was statistically significant for all quantitative density measures ($P < .001$). Furthermore, in the logistic regression models estimating the odds of high density, the interaction of race and BMI was also statistically significant for all quantitative density measures ($P \leq .01$). Therefore, logistic regression models were stratified by BMI (Table 5). Models adjusting for age only and age and BMI are displayed in Supplementary Table 1 (available online). After accounting for age, BMI, and breast cancer risk factors, there was no statistically significant racial difference in the odds of high density using BI-RADS density for nonobese (OR = 1.01, 95% CI = 0.88 to 1.17, $P = .86$) or obese women (OR = 1.00, 95% CI = 0.78 to 1.26, $P = .97$). However, for all quantitative breast density measures, black women had statistically significantly greater odds of high breast density than white women. Specifically, for dense area, black women had 40% to 51% higher odds of high density than white women (nonobese: OR = 1.40, 95% CI = 1.23 to 1.60, $P < .001$; obese: OR = 1.51, 95% CI = 1.28 to 1.77, $P < .001$). For area percent density, black women had 18% to 26% higher odds of high breast density than white women (nonobese: OR = 1.18, 95% CI = 1.02 to 1.37, $P = .03$; obese: OR = 1.26, 95% CI = 1.04 to 1.53, $P = .02$). For dense volume, black women had 27% to 55% higher odds of high breast density than white women (nonobese: OR = 1.27, 95% CI = 1.10 to 1.45, $P = .001$; obese: OR = 1.55, 95% CI = 1.30 to 1.85, $P < .001$). Finally, for volume percent density, black women had 32% to 65% higher odds of high breast density than white women (nonobese: OR = 1.32, 95% CI = 1.15 to 1.52, $P < .001$; obese: OR = 1.73, 95% CI = 1.45 to 2.05, $P < .001$).

Table 3. Distribution of BI-RADS breast density by race

BI-RADS density	White (n = 4216) No. (%)	Black (n = 5282) No. (%)	*P**
1 Almost entirely fatty	315 (7.5)	980 (18.6)	<.001
2 Scattered fibroglandular Densities	2177 (51.6)	3140 (59.5)	
3 Heterogeneously dense	1594 (37.8)	1107 (21.0)	
4 Extremely dense	130 (3.1)	55 (1.0)	

*P values from two-sided Chi square test. BI-RADS = Breast Imaging-Reporting and Data System.

Table 4. Distributions of quantitative breast density measures by race

Quantitative breast density	Mean (SD)	Mean (SD)	*P**
Dense area, cm^2	22.3 (12.3)	22.2 (11.3)	.03
Area percent density, %	17.1 (10.8)	12.3 (7.8)	<.001
Dense volume, cm^3	196.1 (136.5)	266.9 (185.7)	<.001
Volume percent density, %	11.6 (7.7)	9.8 (5.5)	<.001

*P values from two-sided Wilcoxon rank-sum tests.

Discussion

We observed statistically significant differences in breast density for black and white women in a large screening mammography cohort. When quantitative breast density measures were examined, black women had higher breast density than whites after accounting for age, BMI, HRT use, age at menarche, menopause status, family history of breast or ovarian cancer, parity, and age at first birth while there was no statistically significant difference in BI-RADS density.

The BI-RADS categories and area percent density are the most widely used metrics to assess breast density. A recent meta-analysis found that both dense area and area percent density are strong risk factors for breast cancer though the association was stronger for percent density (54). However, it is unclear whether these two-dimensional measures fully capture the variation in breast tissue volume and composition across individuals, and therefore efforts have been most recently geared towards developing fully automated, quantitative volumetric methods, which could provide a more accurate representation of the dense breast tissue (50,55–59). Our study therefore examines both established area-based and novel volumetric quantitative breast density measures, which are shown to be correlated with breast cancer risk (46,60). To the best of our knowledge, this is the largest study to specifically examine breast density among black women while also quantitatively measuring both area and volume density.

The vast majority of studies investigating breast density have been performed in predominantly white or European populations, and it may be possible that volumetric breast density measures may be more sensitive for risk stratification in black women, given the large differences in breast size and BMI between black and white populations (36). Breast density, specifically BI-RADS density, has also been associated with breast cancer risk in black women. However, the magnitude of this association was smaller for black compared with white women in two large studies (30,61). Interestingly, we observed higher density for black women across all quantitative measures even after adjusting for factors known to be associated with density. These racial differences could be because of differences in hormonal exposures across life-course for black and white women (62–65), genetic differences (16–19), or other unmeasured factors.

Our results highlight the importance of carefully controlling for confounding factors, particularly BMI, when comparing breast density by race. We found a statistically significant interaction between race and BMI on density and therefore subsequently performed analyses stratified by BMI. Our findings are consistent with three prior studies that found higher breast density among black compared with white women (22,23,26), two of which adjusted for age, BMI, and reproductive factors (22,26). All three of these studies included fewer than 1000 black women; two examined area percent density (23,26) and the third only BI-RADS density (22). Several additional studies found black women to have similar or lower breast density than whites using BI-RADS density or area percent density (24,25,27–31), but only two studies (27,29) adjusted for age, BMI, and reproductive factors. In general, BMI has been shown to be inversely associated with percent density measures, partly because women with higher BMIs tend to have larger breasts with more non-dense tissue. However, while higher BMI has also been associated with lower dense area in several studies (16), our results suggest that there is an interplay between race, BMI, and both area-based and volumetric breast density measures, indicating the need to better understand how to best measure and interpret density quantitatively in diverse populations.

A small proportion of women in our study were classified as having extremely dense breasts by BI-RADS (3.1% of white and 1.0% of black women). This is lower than some of the estimates reported by other studies, including the Breast Cancer Surveillance Consortium (BCSC), where 7.3% to 8.5% of women undergoing screening mammography from 2000 through 2009 in the United States were classified as having extremely dense breasts (66). However, our results are consistent with previous studies both from our site (67) and from another large study performed in Vermont (42). This variation could be because of differences in populations across sites and/or differences in radiologists' practices. The small proportion of women in the extremely dense category could be partly because of the high prevalence of obesity at our institution, particularly among black women, or the differences in the age distributions of women screened across sites. In addition, BI-RADS density is known to have modest inter-radiologist reliability (68,69), and our lower prevalence of women with extremely dense breasts

Table 5. Logistic regression of having dense breasts by race after adjusting for age, BMI, and breast cancer risk factors*

Outcome and characteristics	OR (95% CI)	P†
BI-RADS density (category 3-4 vs 1-2)		
BMI $<30\,kg/m^2$		
Black vs white	1.01 (0.88 to 1.17)	.86
Age	0.95 (0.94 to 0.96)	<.001
BMI	0.81 (0.79 to 0.82)	<.001
BMI $\geq30\,kg/m^2$		
Black vs white	1.00 (0.78 to 1.26)	.97
Age	0.96 (0.95 to 0.97)	<.001
BMI	0.87 (0.85 to 0.89)	<.001
Dense area (Q3-4 vs Q1-2)		
BMI $<30\,kg/m^2$		
Black vs white	1.40 (1.23 to 1.60)	<.001
Age	0.98 (0.97 to 0.98)	<.001
BMI	0.88 (0.86 to 0.90)	<.001
BMI $\geq30\,kg/m^2$		
Black vs white	1.51 (1.28 to 1.77)	<.001
Age	0.98 (0.98 to 0.99)	<.001
BMI	1.03 (1.02 to 1.05)	<.001
Area percent density (Q3-4 vs Q1-2)		
BMI $<30\,kg/m^2$		
Black vs white	1.18 (1.02 to 1.37)	.03
Age	0.97 (0.96 to 0.98)	<.001
BMI	0.71 (0.70 to 0.73)	<.001
BMI $\geq30\,kg/m^2$		
Black vs white	1.26 (1.04 to 1.53)	.02
Age	0.98 (0.97 to 0.99)	<.001
BMI	0.90 (0.88 to 0.91)	<.001
Dense volume (Q3-4 vs Q1-2)		
BMI $<30\,kg/m^2$		
Black vs white	1.27 (1.10 to 1.45)	.001
Age	0.97 (0.96 to 0.97)	<.001
BMI	1.10 (1.08 to 1.13)	<.001
BMI $\geq30\,kg/m^2$		
Black vs white	1.55 (1.30 to 1.85)	<.001
Age	0.97 (0.96 to 0.98)	<.001
BMI	1.13 (1.11 to 1.15)	<.001
Volume percent density (Q3-4 vs Q1-2)		
BMI $<30\,kg/m^2$		
Black vs white	1.32 (1.15 to 1.52)	<.001
Age	0.95 (0.95 to 0.96)	<.001
BMI	0.81 (0.79 to 0.83)	<.001
BMI $\geq30\,kg/m^2$		
Black vs white	1.73 (1.45 to 2.05)	<.001
Age	0.97 (0.97 to 0.98)	<.001
BMI	1.02 (1.01 to 1.04)	<.001

*Additionally adjusted for current hormone replacement therapy use, age menarche, menopause status, first-degree relative breast or ovarian, age first birth. BI-RADS = Breast Imaging-Reporting and Data System; BMI = body mass index; CI = confidence interval; OR = odds ratio; Q = Quartile.

†P values from Wald tests. All statistical tests were two-sided.

may also reflect differences in radiologist interpretation across sites and populations.

The question of the most useful metrics for breast density assessment has become increasingly important, as it has direct implications for personalized screening. If BI-RADS categories alone are used to identify which women have dense breasts, black women would be less likely than whites to be considered as having dense breasts and therefore not triaged to supplemental screening. Black women have higher breast cancer mortality than white women, are diagnosed with later stage disease, and have higher incidence of poor prognosis and triple-negative breast cancers (20,21), making early detection critical. If black women have a greater quantity of dense breast tissue than whites once BMI is accounted for, this may have implications for their breast cancer risk. To date, density has been associated with breast cancer risk regardless of tumor subtype (70) though there is some evidence that the association is stronger for estrogen receptor–negative cancers and large tumors (71). Existing studies of screening performance have primarily assessed the association of BI-RADS density with screening sensitivity and interval cancers (72–76) while there is little data on quantitative breast density measures and sensitivity of screening mammography (13,71,77). Quantitative measures could alleviate issues of reproducibility of subjective BI-RADS

ARTICLE

measurements; however, it is unknown which quantitative measure is best at predicting screening outcomes or cancer diagnosis. These data emphasize the need to further investigate breast density measurements and their relationship to both screening and cancer outcomes if breast density will be used in large-scale policy interventions for breast cancer prevention and early detection.

A few limitations should be considered when interpreting our findings. First, BMI was obtained from medical records at the time of mammography screening or shortly before and may have been a combination of both self-report and measured weight and height. We excluded women with missing BMI data, though this was less than 5.0% of the baseline study population, and no statistically significant differences in race distribution or breast density levels for women missing BMI were observed. There was also a large number of statistical comparisons performed in our study. However, using a Bonferroni-corrected statistical significance level of .005 (ie, for 10 comparisons), the racial difference would not be statistically significant for area percent density, but the racial difference in all other quantitative measures would remain statistically significant. Though we found statistically significant racial differences across all quantitative breast density measures examined, additional work is needed to determine which measure is most strongly associated with breast cancer risk and most useful for making personalized screening recommendations.

Our study also has several strengths. To the best of our knowledge, this is the largest study to quantitatively assess breast density in black women using digital mammography. Over half of our study population was black, which provided statistical power to compare density levels by race while accounting for important confounders such as age, BMI, and reproductive risk factors. We had digital mammograms for the entire cohort of women undergoing screening mammography for one contiguous year at our institution along with detailed data on breast cancer risk factors such as BMI, reproductive history, family history, and HRT use.

In summary, we found that there was no statistically significant difference in BI-RADS density between black and white women after accounting for age, BMI, and breast cancer risk factors. However, when quantitative measures were used to assess breast density, black women had statistically significantly higher breast density than white women across all quantitative area-based and volumetric density measures examined. Future work will assess how quantitative breast density measures relate to breast cancer outcomes and whether more comprehensive measures of breast density patterns, such as parenchymal texture and complexity, could further explain racial differences in breast cancer incidence, tumor subtype, and stage at diagnosis.

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Notes

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The publicly available LIBRA breast density estimation software tool used in this study can be downloaded at https://www.cbica.upenn.edu/sbia/software/LIBRA/index.html.

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